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Invited Perspectives

Symmetrization in jellyfish: reorganization to regain function, and not lost parts

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ABSTRACT

We recently reported a previously unidentified strategy of self-repair in the moon jellyfish *Aurelia aurita*. Rather than regenerating lost parts, juvenile *Aurelia* reorganize remaining parts to regain essential body symmetry. This process that we called symmetrization is rapid and frequent, and is not driven by cell proliferation or cell death. Instead, the swimming machinery generates mechanical forces that drive symmetrization. We found evidence for symmetrization across three other species of jellyfish (*Chrysaora pacifica*, *Mastigias* sp., and *Cotylorhiza tuberculata*). We propose reorganization to regain function without recovery of initial morphology as a potentially broad class of self-repair strategy beyond radially symmetrical animals, and discuss the implications of this finding on the evolution of self-repair strategies in animals.

For centuries, casual observers and noted experimentalists alike have marked the seemingly miraculous capacity of some organisms to self-repair. In 1740, the naturalist Abbé Trembley performed a series of amputation experiments on the then little-known fresh water polyp, hydra, and watched as it regenerated (Morgan, 1901). He studied this process in much the same way that we do today, by injuring organisms and seeing how they recover. His observations, and those of his contemporaries, ignited something of a fervor, and a field was born.

Since then, many scientists have focused on understanding regeneration mechanisms in several model organisms, where remarkable progress has been made. Our recent work raises the question if there are more varied ways with which the animal world responds to serious injuries. As opposed to regeneration, some organisms are limited to modest wound healing. And recently, working in the moon jellyfish *Aurelia aurita* (Fig. 1A), we described a yet unexplored strategy to respond to injury (Abrams et al., 2015).

We studied the juvenile jellyfish, called ephyra (Fig. 1B). They are typically 3–5 mm in diameter, with eight arms evenly spaced around a disc-shaped body. The symmetrical contraction of the arms is critical for generating fluid vortexes that facilitate propulsion and filter feeding (Sullivan et al., 1997; Higgins et al., 2008). As ephyrae grow into medusae, bell tissue forms between each arm, which takes weeks to months, depending on nutrition abundance.

In response to amputation, we found that instead of regenerating the lost parts, *Aurelia* ephyrae reorganize existing parts, and regain radial symmetry (Fig. 1C–E). This process of reorganization, which we call symmetrization, is fast, often completed in less than 2 days, and occurs at high frequency (~90%). In amputations that leave a large part of the body (Fig. 1D), symmetrization takes longer. In amputations that leave only part of the arms (Fig. 1E), the remaining arms are often resorbed before symmetrization begins. Symmetrization seems to be advantageous, since ephyrae that symmetrized continued growing into symmetrical medusae, while ephyrae that did not symmetrize were unable to swim, and developed abnormally.

The mechanism driving symmetrization is unusual. We found that symmetrization is not driven by cellular processes that usually take place in regeneration, such as cell proliferation or cell death (Huynh et al. (2011); Teng and Toyama, 2011; Mao et al., 2013). Nor is it accomplished through the regeneration of the original muscle architecture, which we could block using cytochalasin D without preventing symmetrization. Instead, symmetry recovery is driven by mechanical forces generated by the propulsion machinery. Inhibiting the excitation–contraction coupling or the skeletal myosin II blocked symmetrization.

To understand how mechanical forces drive symmetrization, we developed a mathematical model that describes the forces driving propulsion, i.e., muscle contraction and elastic response from the jellyfish body. Simulation of the model shows that interactions between these local forces, within the ephyra geometry, can indeed lead to a recovery of global symmetry. Further, by making

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the ephyrae pulse faster or slower, we confirmed that the rate of muscle contraction dictates symmetrization speed.

Therefore, in moon jellyfish, the very machinery that facilitates propulsion and prey capture, also simultaneously enables the sensing and repair of injury. In other words, self-repair in moon jellyfish utilizes constitutively active physiological processes, rather than activating a specialized module. Self-repair in moon jellyfish drives recovery of essential functions, without making new parts. In this context, it is also interesting that unlike sponges, the cnidarians have evolved muscle cells (i.e., as modified epitheliomuscular cells) (Arai, 1997), and in jellyfish, they are organized in such a way that they facilitate self-repair and reorganization.

There is evidence that reorganizing existing parts to recover function, rather than regenerating lost parts, may be a more pervasive strategy across animals. We observed evidence for symmetrization in other jellyfish of this class, i.e., in the ephyrae of the sea nettle *Chrysaora pacifica*, the Mediterranean jellyfish *Mastigias* sp., and the fried egg jellyfish *Cotylorhiza tuberculata*. We also found indications in the literature for the presence of symmetrization in other marine invertebrates. In 1897, Charles Hargitt reported that some hydromedusae do not regenerate, but "recast themselves into a morphological equivalent of their original form" (Hargitt, 1897). A few decades later, Coonfield saw something similar in ctenophores (Coonfield, 1936). Moreover, in 1916, Zirpolo observed that some sea stars that lost an arm and part of the disk recovered to "resemble a nearly perfect four-armed specimen" – perhaps in place of or preceding regeneration (Zirpolo, 1917; Hotchkiss, 1979). These organisms have different morphologies, tissue compositions (i.e., no mesoglea), and have distinct locomotor machineries. Hence, symmetrization may be present beyond Cnidaria, though it could be implemented with different mechanisms in different organisms.

Beyond radially symmetrical animals, we can imagine that fast reorganization to regain function may also be employed in bilateral animals, though perhaps not as dramatically as on the whole organismal scale. At the tissue and organ level, there are a large number of structures that have been observed to regain lost function, at least partially, through remodeling. We know, for instance, that in response to some spinal cord injury, corticospinal tract

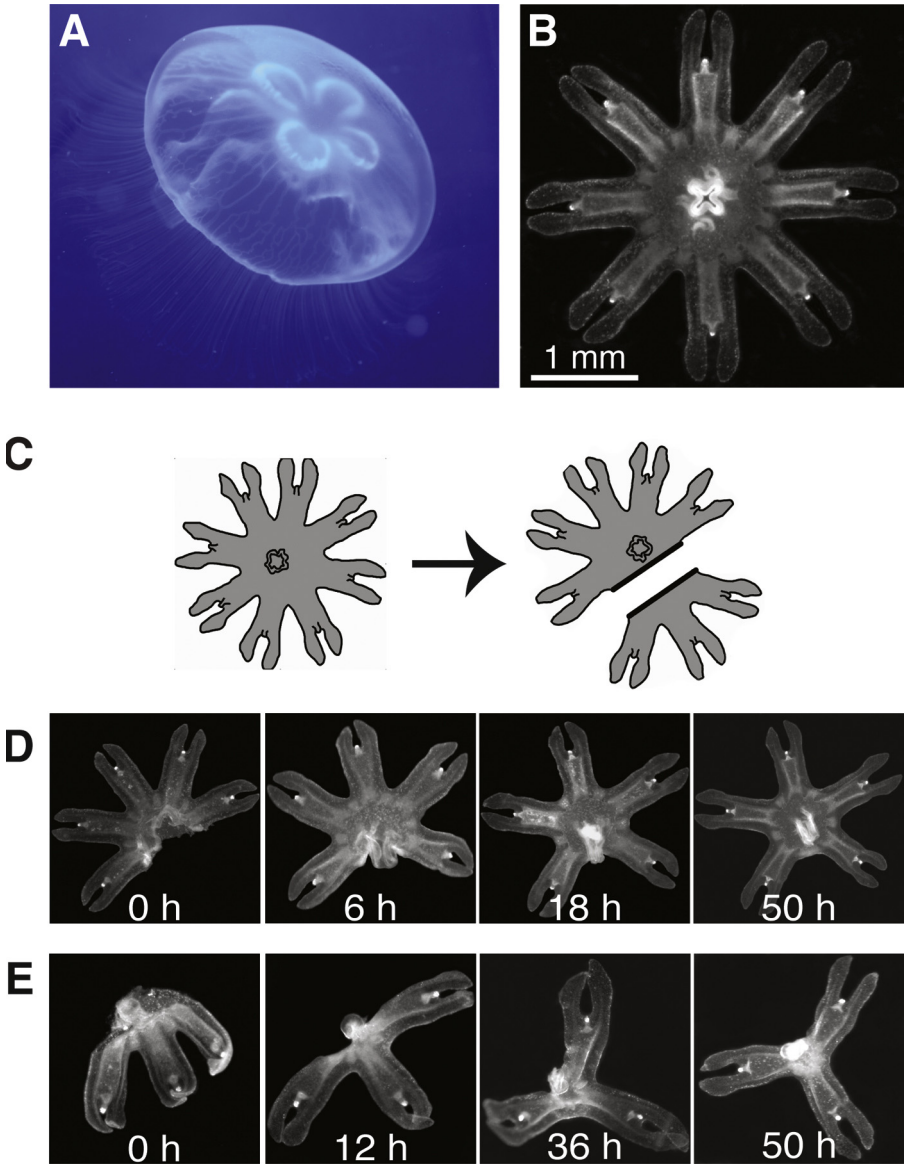

Fig. 1. In response to injury, *Aurelia* ephyrae reorganize existing parts and regain radial symmetry. (A) *Aurelia* medusa (image courtesy of Ty Basinger). (B) *Aurelia* ephyra. (C) An example of amputation schemes used in the study of *Aurelia* self-repair. (D and E) An ephyra was cut into one three-armed and one five-armed ephyra. In this instance, within 2 days, neither regenerated the lost arms, and instead both reorganized to regain radial symmetry.

fibers reorganize to allow recovery of dexterous movements in primates (Nakagawa et al., 2015). A similar overarching strategy of reorganization is also employed by neurons in the brain after a stroke (Dimyan and Cohen, 2011), and by muscle spindle fibers after spinal cord injury (Takeoka et al., 2014). These strategies may be analogous to what we see in jellyfish, in the sense that they both reorganize existing parts to regain lost function. Moreover, the similarity may extend to the underlying mechanism, as mechanical forces have been implicated in the reorganizing of neurons (Tyler, 2012), blood vessels (Senger and Davis, 2011), bones (Crockett et al., 2011), and muscle (Takeoka et al., 2014).

Finally, it is interesting that symmetrization has evolved in organisms that also regenerate. *Aurelia* polyps are known to be capable of regenerating, as are the polyps of many other cnidarians. Did symmetrization evolve in parallel with regeneration, or is this a potentially competing mechanism? How common is it for an organism to have the ability to regenerate in one developmental life stage, and yet reorganize, rather than regenerate, at a different stage? How is the switch between these alternative self-repair mechanisms regulated? Further, might it be possible to induce a switch between these two strategies of self-repair? Understanding the evolutionary relationship between the fundamentals of symmetrization and regeneration might give insights into the adaptive pressures that govern self-repair strategies in animals.

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